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INTERVIEW OUTLINE

USSN 09/485,245

Hopkins "COMPOSITIONS COMPRISING RANDOM MIXTURES OF NUCLEOTIDES"

2:30 am Tuesday, July 10, 2001

Examiner Cynthia Wilder, Ph.D. Crystal Mall I (7th Floor Reception) 703-305-1680

1. APPLICANT'S INVENTION:

a. State of the Prior Art:

- i. The invention relates to an improvement in random priming methods where random sequence oligonucleotides are used to prime DNA synthesis on denatured template DNA at numerous sites along its length. The primer-template complex serves as a substrate for the "Klenow" fragment of DNA polymerase I and radioactive nucleotides are provided such that newly synthesized DNA is made radioactive.
- ii. Various kits containing solutions of oligonucleotids are known for practice of random priming methods. While Sukanuma suggests that shorter primers may have better detection efficiencies than longer primers that suggestion has not been adopted by the art. Instead, the art has tended to prefer kits comprising mixtures of solutions of 9-mers over shorter oligos such as 6-mers because 9-mers achieve better and more rapid priming of a target than do 6-mers.
- iii. More recently, the art has also disclosed kits comprising oligo primers which have been freeze-dried to maintain their stability. The art also teaches that 9-mers and longer oligos are preferred for use in these dried kits.

b. Applicant's Invention-

The present invention is directed to dried mixtures of random primers and relates to the discovery that self-annealing occurs when random 9-mers are used in dried predisposed labeling kits. The problem is specific to 9-mers (and longer oligonucleotides) used in dried kits and does not represent a problem with shorter dried primers.

2. OUTSTANDING REJECTIONS

- a. The previous rejections under 35 U.S.C. §§112 (second paragraph) 102(a) and 103(a) have all been withdrawn.
- b. Claims 1-6 stand rejected under 35 U.S.C. §103(a) Over Sukanuma in view of Shen.
- c. Claim 6 stands rejected under 35 U.S.C. §103(a) over Sukanuma in view of Shen in view of Hoeltke.

3. PATENTABILITY ARGUMENTS

- a. The obviousness rejections under 35 U.S.C. §103(a) should be withdrawn because (1) the selection of 6-mers to 8-mers does constitutes a critical range and (2) the art fails to teach the unexpected results obtained by use of dried 6-8 mers.
 - i. Applicant's examples demonstrate a critical difference in self-priming activity and labeling intensity between 6-8 mers and 9-mers.
 - ii. While Suganuma suggests that the use of 9-mers or longer reduces the priming efficiency of the random primer reaction, the prior art generally taught that longer primers were preferred because longer primers have higher melting temperatures (are more specific).
 - iii. Even if it is accepted that Suganuma suggests the use of shorter primers in kits comprising primers in solution (and it does not) there is no reason to believe that shorter primers would be advantageous in freeze-dried kits that are inherently more stable.
 - iv. Suganuma fails to make any disclosure regarding dried reagents and Shen fails to suggest any reason why the primers of Suganuma should be dried much less why dried 6-8 mers would be superior to dried 9-mers.